REMARKS

The Indefiniteness Rejections and the Rejection under § 101

Claims 4 and 6 are cancelled without prejudice or disclaimer.

The amendments overcome the rejections to the form of the claims.

R^5 and the second choice for R^6 were alleged to be divalent, while should be monovalent. The rejection appears to be over the terms alkylene and cycloalkylalkylene. These groups are not defined to be divalent. They are groups that contain a double bond and are bonded to the rest of the compound at one point, i.e., are monovalent.

The First Enablement Rejection

The Office Action alleges that the specification does not enable the treatment of cardiovascular disorders generally while citing several of the factors from *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

However, even before one gets to the *Wands* factors, the courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated. The disclosure "*must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statement contained therein, which must be relied on for enabling support." See *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). No such evidence or reason for doubting Applicants' disclosure is provided.

Doubt has been held reasonable where, for example, the invention has been characterized as "highly unusual," *In re Houghton*, 433 F.2d 820 (CCPA 1970), as "incredible," *In re Citron*, 325 F.2d 248, (CCPA 1963), or as "too speculative," *In re Eltgroth*, 419 F.2d 918 (CCPA 1970). The treatment of cardiovascular diseases is not objectively doubtable, i.e., not "highly unusual," "incredible," and/or "too speculative." Thus, the rejection should be withdrawn for this reason alone.

Nevertheless, applicants address the *Wands* factors discussed by the Office Action.

The Office Action alleges that the scope of the claims covers millions of compounds and a vast array of diseases. No separate enablement rejection is made over the compound claims.

Thus, as a premise, the compounds are considered enabled. With respect to the alleged vast array of diseases, the Patent Office has not provided any reason why one of ordinary skill in the art would not be able, through routine screening and testing, to determine which of the synthesized compounds according to the claims possesses beneficial properties to any of the specific diseases encompasses by the claims. Screening and testing of thousands of compounds in a variety of assays in this field of art is routine, and thus, does not constitute undue experimentation, especially in view of the guidance provided by the specification on page 2, lines 20-39, wherein applicants cite to several references that teach how to test the activity levels of the claimed compounds.

Additionally, applicants provide guidance as to the type of activity the claimed compounds possess. The specification teaches that the compounds of formula I exhibit specific inhibition of cGMP phosphodiesterase (PDE V). See specification on page 2, lines 14-18. The specification further teaches that "compounds of the formula I and their physiologically acceptable salts can be used in the control of diseases in which an increase in the cGMP (cyclic guanosine monophosphate) level leads to inhibition or prevention of inflammation and muscle relaxation. The compounds according to the invention can particularly be used in the treatment of diseases of the cardiovascular system and for the treatment and/or therapy of potency disorders." See page 12, line 33 to page 13, line 2.

Thus, any one of the claimed compounds can be tested by routine protocol known to those of ordinary skill in the art. As stated by the court in *Wands*, supra, a considerable amount of experimentation is permissible, if it is merely routine, which it is, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed, which it does.

The Office Action also alleges that no specific biological data is provided, i.e., there are no working examples to the treatment of any disorder. However, the law does not require an applicant to test a compound in examples. See, for example, *Marzocchi*, supra, stating that whether "an enabling teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance." The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

Additionally, with respect to pharmaceutical inventions, the courts have specifically decided that an applicant is not required to test the claimed compounds in their final use in order to enable their use. The Federal Circuit in *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), stated that

> usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful can be well before it is ready to be administered to humans. If the courts were to require Phase II testing in order to prove utility for pharmaceutical inventions, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas.

While no specific biological results are provided in the specification, the Office Action alleges that physiological data is generally considered to be an unpredictable factor, while citing *In re Fisher*, 427, F.2d 833, 166 USPQ 18 (CCPA 1970). The court in *Fisher* does not state or even suggest that physiological data is considered to be an unpredictable factor. Instead the position of the courts is the opposite. In *Cross v. Iizuka*, 224 USPQ 739 (Fed. Cir. 1985), the court stated that "*in vitro* results with respect to the particular pharmacological activity are generally predictive of *in vivo* tests results, i.e., there is a reasonable correlation therebetween. Were this not so, the testing procedures of the pharmaceutical industry would not be as they are."

The Office Action alleges that the direction and guidance provided is limited to dosages that are generic as to disease. Applicants respectfully disagree. As discussed above, applicants have provided guidance as to type of activities possessed by the claimed compounds and guidance as to how testing of prepared species should be tested for activity levels.

Additionally, with respect to the disclosure of dosages, the Federal Circuit in *Cross,* supra, affirmed a USPTO Board of Patent Interferences decision on whether dosage levels need to be disclosed for a pharmaceutical in order to enable it. The Federal Circuit held that where sufficient credible evidence that one skilled in the art, without the exercise of inventive skill or undue experimentation, could determine dosage levels, disclosure of dosage levels is not necessary for enablement.

The Manual of Patent Examination and Procedure, is in accord with the *Cross* decision. The MPEP states that it is unnecessary to disclose dosages to satisfy the enablement requirement. See, *e.g.*, MPEP 2164.01(c): "it is not necessary to specify the dosage ... if it is known in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on

knowledge of compounds having similar physical or biological activity would be able to discern an appropriate dosage ... without undue experimentation, this would be sufficient to satisfy 35 U.S.C. §112, first paragraph."

Applicants thus, by providing specific guidance as to appropriate dosage levels and modes of administration even go further than necessary to provide an enabling disclosure. See specification on page 12, line 1 to page 13, line 16. A disclosure of dosages, or actually a disclosure of how to obtain dosages, was held to be evidence supporting enablement. In *Cf. United States v. Telectronics, Inc* ., 857 F.2d 778, 785, 8 USPQ2d 1217 (Fed. Cir. 1988) the court found a specification enabling in part because those skilled in the art would know how to conduct a dose response study to determine the appropriate amounts to be used. In the present application applicants do more. They disclose specific doses to be administered.

Applicants bring the attention of the Examiner to a case having similar facts to the current case. In *In re Bundy*, 209 USPQ 48, (1981), the specification as enabling disclosure provided that the compounds of the invention possess activity similar to E-type prostaglandins. The court held this disclosure sufficient by stating that "what is necessary to satisfy the how-to-use requirement of section 112 is the disclosure of some activity coupled with knowledge as to the use of this activity." Similarly here, applicants teach the type of activity possesses by the claimed compounds and also provide guidance as to testing their activity levels. This amount of disclosure is sufficient to enable the claimed method.

Supplementally, the Patent Office allows numerous applications directing claims to the treatment of cardiovascular disorders or diseases. See, for example, recently (less than a week) allowed applications, US 6,613,897 (claim 21), US 6,613,804 (claim 6), US 6,613,772 (claim 4), and 6,613,757 (claim 4), among many hundreds of patents having claims of similar scope. All the allowed patents having claims of similar scope are presumed valid, and thus, enabled. Similarly, the current claims should be found enabled as well.

Applicants provide ample evidence to the claimed activity and ample guidance to test the activity of further compounds according to the invention. Any one of the claimed compounds can be tested by routine protocol known to those of ordinary skill in the art, i.e., their testing is does not constitute undue experimentation. Thus, the claims are enabled.

Reconsideration is respectfully requested.

The Second Enablement Rejection

The Office Action alleges that the specification does not enable any person skilled in the art to prepare solvates of the claimed compounds.

Applicants respectfully disagree. While no solvate is exemplified, one of ordinary skill in the art based on the guidance provided by the specification without undue experimentation could prepare a solvate. The specification on page 4, line 29 to page 5, line 3, teaches that

> solvates of the compounds of the formula I are understood as meaning adducts of inert solvent molecules to the compounds of the formula I which are formed on account of their mutual attractive force. Solvates are, for example, mono- or dihydrates or alcoholates.

One of ordinary skill in the art, can bring together any number of solvents with a compound of formula I and determine whether a solvate is formed.

The Office Action alleges that "the dozens of examples all failed to produce a solvate" and that "there is no evidence that solvates of these compounds actually exist; if they did, they would have formed."

The examples referred to were not directed to the preparation of solvates of the claimed compounds. Thus, there is no "failure" to prepare a solvate, or basis for the allegation that if solvates actually exist, they would have formed. The specification teaches that solvates exist, and even further teaches that exemplary solvates are mono- or dihydrates or alcoholates (see above). There is no basis for doubting applicants' disclosure.

The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). The disclosure must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statement contained therein. See *In re Marzocchi*, supra. No such evidence or reason for doubting Applicants' disclosure is provided.

Doubt has been held reasonable where, for example, the invention has been characterized as "highly unusual," *In re Houghton*, 433 F.2d 820 (CCPA 1970), as "incredible," *In re Citron*, 325 F.2d 248, (CCPA 1963), or as "too speculative," *In re Eltgroth*, 419 F.2d 918 (CCPA 1970). Because compounds having similar activities are known in the art, the existence of a new class of compounds having the claimed activities is not objectively doubtable, i.e., not "highly unusual," "incredible,"

and/or "too speculative." The formation of a solvate to a compound that is enabled is not "highly unusual," "incredible," and/or "too speculative," since thousands of compounds have or form solvates.

Additionally, "the [enablement] requirement is satisfied if, given what they [, those or ordinary skill in the art,] already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" See *Amgen v Hoechst Marion Roussel*, 65 USPQ2d 1385 (CA FC 2003). Explicitly providing examples for preparing solvates is not necessary to enable the same. See, for example, *Spectra-Physics v Coherent*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987) ("A patent need not teach, and preferably omits, what is well known in the art"); *In re Howarth,* 654 F.2d at 105, 210 USPQ 689 (CCPA 1981) ("An inventor need not ... explain every detail since he is speaking to those skilled in the art."); *In re Gay*, 309 F.2d 769, 774, 135 USPQ 311 (CCPA 1962) ("Not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be.") One of ordinary skill in the art can without undue experimentation prepare solvates of the claimed compounds.

The only apparent reason for the rejection is the lack of examples specifically illustrating the formation of solvates. However, examples are not required to enable an invention. Instead there is no requirement for <u>any</u> examples. See, for example, *Marzocchi*, supra, stating that "an enabling teaching is set forth, either <u>by use of illustrative examples or by broad terminology, is of no importance</u>." The MPEP also agrees by stating that "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, <u>does not turn on whether an example is disclosed</u>." See MPEP § 2164.02.

The PTO has failed to meet its burden of establishing that the disclosure does not enable one skilled in the art to make the compounds recited in the claims. Instead of relying on proper probative evidence, the rejection is improperly based on the bare allegation that the disclosure does not provide examples where solvates are formed. No evidence has been presented which would demonstrate that the guidance provided by the specification or what was already known in the prior art at the time of filing this application is inadequate to enable the preparation of the claimed solvates without undue experimentation.

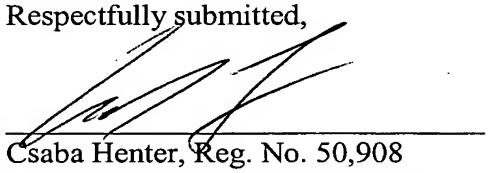
Nevertheless, applicants to further the prosecution of this application have removed the

term solvates from claim 1 and its dependent claims and have directed new claims 13 and 14 only to said solvates.

Reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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